REMARKS

The Office Action mailed on December 5, 2000, has been received and reviewed. Claims 1, 2, 8, and 12-29 are currently pending in the application. Claims 1, 2, 8 and 12-18 stand rejected. Reconsideration of the application is respectfully requested in light of the amendments and remarks presented herein.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 12-13 and 24-25 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, each of claims 12, 13, 24, and 25 was rejected for reciting "a capillary column". It is the Office's position that the recitation of "a capillary column" in these claims did not have proper antecedent basis. Claims 12 and 13 have been amended to replace the recitation of "a capillary column" with --said porous capillary column-- and claims 24 and 25 have been amended to replace "a capillary column" with --said capillary column--, referring back to the capillary column previously recited in the independent claims from which each of claims 12, 13, 24, and 25 respectively depends. It is respectfully submitted that these amendments to claims 12, 13, 24, and 25 do not change the scopes of any of these claims.

It is respectfully submitted that each of claims 12, 13, 24, and 25, as amended, is in condition for allowance. Accordingly, it is respectfully requested that the Office withdraw the rejections of each of these claims under the second paragraph of section 112.

Rejections Under 35 U.S.C. § 102(b)

Claims 1, 2, 8, 14-16, 18-20, 22, 23, and 26-28 stand rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent 5,482,598 to Isaka et al. (hereinafter "Isaka").

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Brothers v.*

Union Oil Co. of California, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The identical invention must be shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

Isaka discloses a chromatic separation device that includes a silicon substrate and a single porous microchannel formed therein, as well as methods for fabricating and using the chromatographic separation device. The chromatographic separation device disclosed in Isaka and illustrated in FIGs. 1-3 thereof includes a porous column 21, 45 to which a sample is applied through an inlet port 11, 42. As the sample moves through the porous column 21, 45, various components of the sample may be separated from one another. An enzyme may be disposed at some point along the length of the column to react with a particular component, or analyte, in the sample in such a manner that a detectable reaction product is formed. After exiting the porous channel 21, 45 from an outlet port 12, 43 thereof, portions of the sample, including any detectable product of a reaction between an enzyme and analyte, enter a capillary that communicates with the outlet port 12, 43. The capillary transports these portions of the sample to a detector. See Isaka, col. 5, lines 24-30.

By way of contrast with Isaka, claim 1 recites a separation method which includes, among other things, applying a sample to an end of a porous capillary column that includes a matrix and at least one capture substrate disposed on the matrix and drawing the sample through the porous capillary column. Claim 1 also recites that, as the sample is drawn through the capillary column, a constituent may be separated from the remainder of the sample "by [the] at least one capture substrate."

Isaka does not disclose a method for using a separation device that includes a capture substrate disposed along the length of a column thereof which separates a constituent from the remainder of a sample. Rather, Isaka merely discloses the use of an enzyme. While an enzyme couples to a substrate, the binding only occurs for a sufficient time for the enzyme to catalyze a chemical change to the substrate, which, in the case of Isaka, results in a detectable and, therefore, measurable reaction product. Isaka provides the examples of use of the enzymes enzyme

invertase, which hydrolyzes saccharose, and uricase, which, as is well known in the art, catalyzes the reaction in which uric acid is converted to allantoin. Isaka, col. 3, lines 6-11. Moreover, Isaka does not disclose that the measurable reaction product is separated from the remainder of the sample. Rather, the reaction product exits the capillary column through the outlet port 12, 43 with the remainder of the sample, then enters a capillary with the remainder of the sample, where the presence of the reaction product in the remainder of the sample may be detected.

For these reasons, it is respectfully submitted that Isaka does not anticipate each and every element recited in claim 1. Therefore, it is respectfully submitted that, under 35 U.S.C. § 102(b), independent claim 1 is allowable over Isaka.

Claims 2, 8, and 14-16 are each allowable, among other reasons, as depending either directly or indirectly from claim 1, which should be allowed.

Claim 2 is further allowable since Isaka does not disclose "detecting [a] constituent with at least one detector disposed proximate a detecting region of [the] capillary column." Rather, sample constituents, including the products of reactions catalyzed by enzymes disposed along the column of the apparatus disclosed in Isaka, exit the column through an outlet port 12, 43, then enter a capillary, in which the sample constituents may be detected.

Independent claim 18, as amended and presented herein, recites a separation method that includes, among other things, detecting the binding of a constituent and a stationary phase. The binding is detected at the location of a capillary column at which the stationary phase is located.

Isaka does not disclose either "detecting binding" or that binding is detected at the location of a capillary column at which a stationary phase is located. Rather, Isaka discloses that an enzyme, such as enzyme invertase or uricase, may be disposed at some point along the length of a column. As a sample migrates through the column, the enzyme momentarily binds with a substrate in the sample and catalyzes a chemical change to the substrate. The chemically changed substrate, or reaction product, then continues to migrate through the column and exits the column through an outlet port. The sample and any reaction product therein then enter a capillary, within which the reaction product is detected. Thus, the reaction product is not detected while being

bound to the enzyme. Moreover, in Isaka, detection does not occur at the location of the column at which the enzyme is bound.

Therefore, Isaka does not anticipate each and every element of amended claim 18. Accordingly, it is respectfully submitted that, under 35 U.S.C. § 102(b), amended claim 18 is allowable over Isaka.

Claims 19-20, 22-23, and 26-28 are each allowable, among other reasons, as depending either directly or indirectly from claim 18, which should be allowed.

Claim 19 is further allowable since Isaka does not disclose "analyzing [a] detection reagent to determine whether [a] constituent is present." As is well known in the art, a detection reagent specifically binds to an analyte or capture molecule to facilitate detection of the analyte. In contrast, Isaka discloses the use of a fluorescent die to detect bands obtained during electrophoretic separation, which, as those of skill in the art are aware, typically involves the use of a nonspecific fluorescent dye to illuminate all of the electrophoretically separated bands. Moreover, the enzymes disclosed in Isaka are not used as detection reagents, but rather to modify a sample constituent to a detectable form.

Claim 20, which depends from claim 19, is also allowable since Isaka does not disclose "quantifying a change in [a] detection reagent." Rather, Isaka discloses that an enzyme may bind an catalyze the chemical alteration of a constituent of the sample to form a reaction product, which may be detected. The reaction product is not a detection reagent.

For the foregoing reasons, it is respectfully submitted that claims 1, 2, 8, 14-16, 18-20, 22, 23, and 26-28 are allowable under 35 U.S.C. § 102(b). It is, therefore, respectfully requested that the 35 U.S.C. § 102(b) rejections of each of these claims be withdrawn.

Rejections Under 35 U.S.C. § 103(a)

Isaka in View of Sunzeri and Swedberg

Claims 12, 13, 21, 24, and 25 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Isaka in view of U.S. Patent 5,536,382 to Sunzeri (hereinafter "Sunzeri") and U.S. Patent 5,571,410 to Swedberg et al. (hereinafter "Swedberg").

M.P.E.P. 706.02(j) sets forth the standard for a Section 103(a) rejection:

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). (Emphasis added).

The nonobviousness of independent claims 1 and 18 precludes the rejections of claims 12 and 13, which depend from claim 1, and of claims 21, 24, and 25, which depend from claim 18, because a dependent claim is obvious only if the independent claim from which it depends is obvious. *See* In re Fine, 5 U.S.P.Q.2d 1596, 1600 (Fed. Cir. 1988), *see also* MPEP § 2143.03.

Moreover, it is respectfully submitted that one of skill in the art would not be motivated to combine the teachings of Isaka with those of Sunzeri and Swedberg in the manner that has been set forth in the outstanding Office Action.

Sunzeri teaches a method for analyzing the constituents of human biological fluids. A labeled specific binding pair member is added to a human biological fluid to effect binding between an analyte in the human biological fluid and the specific binding pair member. The constituents of the human biological fluid, including complexes of the analyte and the specific binding pair member, are separated by way of known capillary electrophoresis techniques. The separation obtained by way of capillary electrophoresis is then compared to a control, which provides a standard for quantitation by indicating the position where the analyte would have been

present if it had not been bound by the labeled specific binding pair member. The specific binding pair member is not immobilized to the matrix of the capillary electrophoresis substrate, but rather is permitted to travel therethrough with the bound analyte.

Swedberg teaches a miniaturized separation apparatus including a column within which a porous quantity of biocompatible material, such as "nylon, cellulose, polymethylmethacrylate, polyacrylamide, agarose, or the like" may be disposed. Col. 27, lines 37-40. Each of these materials have long been used in separating the constituents of biological samples. Swedberg does not teach that the porous matrix is formed in the substrate. Rather, a quantity of biocompatible, porous material is placed into an open column.

It is respectfully submitted that, none of Isaka, Sunzeri, Swedberg, or the knowledge generally available to one of ordinary skill in the art provides the motivation requisite for combining the teachings of these references and establishing a *prima facie* case of obviousness.

Isaka discloses a separation method that includes chemically altering an analyte to form a reaction product, then detecting the reaction product after the reaction product exits the column with the remainder of the sample. Accordingly, it is respectfully submitted that neither the teachings nor the suggestions of Isaka would have motivated one of ordinary skill in the art to immobilize a capture substrate or stationary phase along the capillary column thereof in such a manner that an analyte would be separated from the remainder of a sample. Moreover, Isaka would not have motivated one of ordinary skill in the art to detect the binding of an analyte to a capture substrate or a stationary phase at the location of the capture substrate or stationary phase.

While Sunzeri teaches binding of an analyte to a complementary specific binding pair member, these elements are bound before being applied to a capillary column and are not detected as a result of separation that occurs as a sample that includes the analyte flows through the capillary column and is bound to a specific binding pair member immobilized thereto. Thus, one of ordinary skill in the art would not be motivated by the teachings or suggestions of Sunzeri to immobilize a stationary phase or a specific binding pair member, or capture substrate, along a

capillary column or to detect binding of an analyte to the stationary phase or capture substrate at the location of the column at which the stationary phase or capture substrate is immobilized.

Although Swedberg teaches a capillary electrophoresis separation device in which that includes an open trench formed in a substrate and filled with a different, synthetic porous material, not with the same material as that from which the substrate is formed. Swedberg also teaches that a specific binding pair member may be secured at some location along the substrate. Nonetheless, Swedberg does not include any teaching or suggestion that would have motivated one of ordinary skill in the art to apply the teachings thereof to a separation method that involves use of a device with a substrate and a porous column formed in the substrate and including a matrix formed from the same material as the substrate.

For these reasons, it is respectfully submitted that one of ordinary skill in the art would not have been motivated to combine the teachings of Isaka, Sunzeri, and Swedberg in the manner that was asserted in the outstanding Office Action.

Furthermore, based on the manner in which the teachings of these references have been combined by the Office, it appears that any such motivation to make the asserted combination could only have been based on the hindsight provided by the disclosure or claims of the referenced application.

For these reasons, withdrawal of the 35 U.S.C. § 103(a) rejections of claims 12, 13, 21, 24, and 25, as being rendered unpatentable over the combination of Isaka, Sunzeri, and Swedberg, is respectfully requested.

Isaka in View of Northrup

Claims 17 and 19 (presumably 29) stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Isaka in view of U.S. Patent 5,882,496 to Northrup et al. (hereinafter "Northrup").

The nonobviousness of independent claims 1 and 18 precludes the respective rejections of claims 17, 19, and, presumably, 29, because a dependent claim is obvious only if the independent

claim from which it depends is obvious. *See* In re Fine, 5 U.S.P.Q.2d 1596, 1600 (Fed. Cir. 1988), *see also* MPEP § 2143.03. Therefore, withdrawal of the section 103 rejections of claims 17, 19, and, presumably, 29 is respectfully requested.

New Claims 30 and 31

New claims 30 and 31 have been added. Claim 30 recites that the capture substrate of claim 1 comprises at least one of an antibody and an antigen, while claim 31 recites that the stationary phase of claim 18 comprises at least one of an antibody and an antigen. It is respectfully submitted that neither claim 30 nor claim 31 adds new matter, as the use of an antibody or an antigen as a capture substrate or a stationary phase are supported by the originally filed specification, at, for example, page 15, lines 18-23.

It is also respectfully submitted that claims 30 and 31 are each allowable as respectively depending from claims 1 and 18, which should be allowed.

CONCLUSION

Claims 1, 2, 8, and 12-31 are believed to be in condition for allowance, and an early notice thereof is respectfully solicited. Should it be determines that additional issues remain which might be resolved by a telephone conference, the Office is respectfully invited to contact the undersigned attorney.

Respectfully submitted,

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